Journal of Social Research

P-ISSN: 2827-9832
E-ISSN: 2828-335x
Vol.4, No.8, August 2025
http://ijsr.internationaljournallabs.com/index.php/ijsr

The Effectiveness of Omega-3 Fatty Acids In Medical Nutritional Therapy For Critically Ill Patients

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ABSTRACT

Malnutrition is a common problem found in hospitals and has a serious impact on the patient's healing process, which can increase morbidity and mortality rates, contributing to a prolonged length of stay and increased treatment costs. Therefore, nutritional support is necessary to prevent malnutrition and further complications, such as those containing polyunsaturated omega-3 fatty acids, specifically *docosahexaenoic acid* (DHA) and *eicosapentaenoic acid* (EPA). These fatty acids have anti-inflammatory, immunomodulatory, and antioxidant effects that have the potential to enhance immunity, repair damaged tissue, and support the maintenance of muscle mass and strength. The purpose of this literature study is to evaluate the effect of providing nutrition containing omega-3, both enterally and parenterally, on the healing process of patients with critical illness. The design of this study is a literature review of research sources using Randomized Controlled Trials (RCTs) and cohort studies. From the results of this literature study, it can be concluded that nutrition containing omega-3 affects accelerating the healing of patients with critical illnesses and reducing the risk of complications, thereby shortening the length of ICU stay.

Keywords: *critical illness; enteral nutrition; parenteral nutrition; omega-3 fatty acids*

INTRODUCTION

Critical illness is a condition that requires special management in the field of nutrition. In these conditions, there is an increase in metabolism and catabolism so that it can trigger malnutrition. This can be influenced by various factors, including the type of disease, the management applied, the quality of services in the intensive care unit (ICU) and multidisciplinary participation (Harti, 2024).

Malnutrition is a problem that is often found in hospitals and has a serious impact on the patient's healing process so that it can increase morbidity and mortality rates which ultimately contribute to the extension of the length of treatment and increase the cost of treatment. The prevalence of malnutrition is reported to range from 20 to 50% in various European and South American countries with an average of 41.7% worldwide (Ouaijan et al., 2023). Research in Turkey reported the number of malnutrition as high as 39% (Ouaijan et al., 2023). Studies conducted on elderly patients in Saudi Arabia showed that 5.3% of participants were severely malnourished, while 32.9% were at risk of malnutrition (Alamri et al., 2025). Other studies show malnutrition in ICUs as high as 78.1% in developing countries and 50% in developed countries (Delfia et al., 2023). The prevalence of malnutrition in Indonesia is estimated to range from 33-70%. Research in the Internal Medicine section of Dr. Hasan Sadikin Hospital found patients with malnutrition of 71.8% and severe malnutrition of 28.9%. Another study at Sumber Waras Hospital Jakarta found that 47.76% of patients were malnourished (Keputusan Menteri Kesehatan RI, 2019).

The impact of malnutrition has the potential to reduce organ function, including digestive disorders such as impaired motility and malabsorption which can trigger a lack of energy and

muscle mass which can lead to morbidity and mortality. To prevent this, nutritional support is needed to prevent malnutrition and further complications that can be given both enterally and parenterally. Some of these types of nutrients contain omega 3 polyunsaturated fatty acids, namely docosahexaenoiacid (DHA) and eicosapentaenoic acid (EPA) (Ouagueni et al., 2024; Stoppe et al., 2024). These fatty acids have anti-inflammatory, immunomodulatory, and antioxidant effects that have the potential to boost immunity and repair damaged tissues and help maintain muscle mass and strength (Pradelli et al., 2025). Therefore, this literature study aims to evaluate the effect of providing nutrients containing omega-3 both through enteral and parenteral pathways on the healing process of patients in critical conditions. It is hoped that the results of this study can contribute to reducing malnutrition, morbidity, and mortality rates within the hospital.

Omega-3 fatty acids, particularly DHA and EPA, have emerged as a promising solution due to their anti-inflammatory, immunomodulatory, and antioxidant properties, which may enhance immunity, repair tissues, and preserve muscle mass (Pradelli et al., 2025). However, existing research presents conflicting results. For instance, Doaei et al. (2021) found that omega-3 improved lung and kidney function in COVID-19 patients, while Singer et al. (2021) observed no significant benefits in lung function for mechanically ventilated patients, despite shorter ICU stays. Such inconsistencies underscore the need for further investigation into the efficacy of omega-3 across different critical conditions, including sepsis, burns, and gastrointestinal disorders, where its effects remain unclear (Weylandt et al., 2023; Cuartero-Corbalán et al., 2024).

This literature review addresses these gaps by synthesizing recent evidence (2021–2025) to evaluate the impact of omega-3 on clinical outcomes, compare enteral and parenteral administration routes, and identify optimal dosing strategies. By doing so, it aims to provide evidence-based recommendations for optimizing nutritional therapy in ICUs. The potential benefits include reduced malnutrition-related complications, faster patient recovery, shorter hospital stays, and cost savings for healthcare systems. Ultimately, this study seeks to contribute to standardized protocols for omega-3 use in critical care, improving patient outcomes and resource utilization.

METHOD

The design of this study was a literature review with a search for literature sources using the PubMed, Springer Link, ScienceDirect, and Google Scholar databases. The study used articles from national and international journals that provided relevant information on the administration of enteral and parenteral nutrition to critically ill patients. Using the Boolean method in the search, 7,696 related journals were found. These results were then screened according to the inclusion and exclusion criteria. Inclusion criteria included a population aged ≥18 years admitted to the ICU with *critical illness* such as sepsis, ARDS, severe trauma, burns, or major postoperative conditions, and interventions involving the administration of enteral and parenteral nutrition containing omega-3 fatty acids without the addition of other micronutrients. Meanwhile, the exclusion criteria included children and outpatients, as well as interventions that did not use omega-3 or involved additional supplements. Based on these criteria, seven journals were comprehensively selected and described in the discussion results from the last five years,

namely 2021–2025. The keywords used in the article search were omega-3, *critical illness*, nutrition, DHA, and malnutrition.

RESULTS AND DISCUSSION

From the search of articles in the database, 7 articles were obtained that were by the objectives of the literature study and the inclusion and exclusion criteria. The results of the article review are listed in Table 1.

Table 1. Summary of the results of the literature study according to the inclusion criteria

Research/ Country	Sample/ Method	Diagnosis	Intervention	Parameter	Result	Conclusion
Doaei et al, 2021/ Iran	128 sample/ Randomized Controlled Trial	COVID-19	Patients in the ICU room aged 35-85 years were given enteral nutrition containing omega-3 (400 mg EPAs, 200 mg DHAs) for 14 days	Arterial blood gas analysis, renal function test, blood glucose, mean artery pressure (MAP), complete blood count, acute physiology and chronic health evaluation II (APACHE II), glasglow coma scale (GCS), electrolyte serum	Increased arterial pH, HCO3, and Be levels and decreased levels of BUN, Cr, and K ($p < 0.05$). There were no significant differences in blood sugar levels, Na, HCT, Ca, P, MAP, O2 saturation, PO2, PCO2, WBCs, GCS, Hb, Plt, PTT, and albumin.	Improvement of kidney function and lung function
Singer et al, 2021/ Israel	100 sample / Randomized Controlled Trial	Patients with an APACHE II score of > 15 who use mechanical ventilation with an REE of no more than 80%	Patients in the ICU room (24 hours after admission) aged 18-35 years were given enteral and parenteral nutrition containing omega 3 for 5 days	Physical examination, SOFA score and incidence of adverse events (AEs), Laboratory (Liver function: ALT, AST, GGT, AP, total bilirubin, direct bilirubin, blood glucose, electrolytes (sodium, potassium, calcium, phosphorus, magnesium), albumin, protein, creatinine, urea and uric acid, prealbumin, CRP, INR, HDL and LDL, triglycerides, cholesterol)	Oxygen levels (PaO2/FiO2 from D1 to D4: -1.3 ± 83.7, n = 42 and 13.3 ± 86.1, n = 39, respectively in the omega-3 and control groups, $p = 0.7795$) and pulmonary function parameters did not differ significantly between groups.	- Shorter ICU stay - Faster sedation - Shorter ventilator usage
El Rhaman et al, 2022/ Egypt	60 sample/ Cohort	Sepsis	Patients aged 18 years with a diagnosis *of mild sepsis* were given omega-3 doses of 9	Length of treatment, mortality, Complete blood count (CBC), current blood	Decreased white blood cell count, Creactive protein, and procalcitonin	- The number of deaths is decreasing, - Short duration of treatment,

Research/ Country	Sample/ Method	Diagnosis	Intervention	Parameter	Result	Conclusion
			grams for 7 days orally/nasogastricly	sugar, BUN, serum Na+, serum K+ and creatinine. Liver function: SGOT and SGPT. serum Mg++, serum Ca++ and PO4, blood culture and *arterial blood gas* (ABG). Microbiological tests: sputum culture, blood, urine) and thoracic photos.	on day 5 (p = 0.001, 0.012, and 0.001) on day 7 (p = 0.014, 0.008, and 0.29)	- No complications
Weyland et al, 2023/ Germany	8 sample / Randomised control trial	Digestive disorders (mesenteric infarction, inflammatory bowel disease, bowel obstruction, trauma)	Patients aged ≥ 18 years were given omega-3 parenterally for 8 weeks	Complete blood cells, liver function, inflammatory markers, serum albumin, lipid profile	EPA plus DHA in erythrocytes (Omega-3 Index) was high with a median of 11.96% at baseline and decreased to 9.57% without omega-3 in PN	There was no significant change in inflammatory markers and clinical outcomes
Zhou et al, 2023/ China	140 sample / Randomised Controlled Trials	Burns with *a total body surface area* (TBSA) of ≥ 30%	Patients aged ≥ 18 years in the hospital were given enteral and parenteral nutrition containing omega 3	Length of treatment, mortality rate, sepsis complications, septic shock and *multiple organ dysfunction syndrome* (MODS), C-reactive protein (CRP), IL-6	Decreased incidence of severe sepsis, septic shock, multiple organ dysfunction syndrome (RR = 0.38, 95% CI [0.19, 0.75], P = 0.005), C-reactive protein levels (MD = 39.70[-81.63, 2.23], P = 0.06), however, there was no difference in 14-day mortality (RR = 1.10, 95%CI [0.59, 2.05], P = 0.75)	- Complications (sepsis, septic shock, and MODS) are lower, - Faster use of mechanical ventilation, - Shorter duration of treatment
Corbalan, et al, 2024/ Spain	54 sample / Randomised Controlled Trials	Acute abdominal disorders	Patients aged ≥ 18 years who will undergo surgery and postoperatively are given omega 3 parenteral nutrition for 7 days	Postoperative complications (hypovolemic shock, systemic inflammatory response syndrome, sepsis. Albumin, prealbumin, transferrin, trigliseride, kolesterol, GGT, AST, ALT	No significant differences were found between groups in clinical parameters and outcomes, oxidative stress, or inflammatory markers	There were no significant differences in clinical outcomes (use of mechanical ventilation, length of treatment and complications)
Berlana et al, 2024/ Spain	69 sample/ Randomised Controlled Trial	COVID-19	Patients ≥18 years old were given parenteral nutrition containing omega 3 for 9 days	C-reactive protein (CRP) and interleukin-6 (IL-6) levels, inflammatory markers (TNF-α, IFN-γ, IL-	Significant decrease in CRP, IL-6 and CXCL10 levels (p<0.05)	- A decrease in the death rate, Shorter ICU stay

Research/ Country	Sample/ Method	Diagnosis	Intervention	Parameter	Result	Conclusion
				1Ra, CXCL10), liver function, triglyceride levels, and clinical externalities such as death and length of ICU and ward stay		

Based on a literature study conducted by Doaei et al in 2021, the administration of enteral nutrition to COVID-19 patients provides improvements in lung function and kidney function as shown by the results of blood gas analysis examinations, namely increased arterial pH, HCO3 and decreased levels of BUN, Cr, and K ($p < 0.05$) (Doaei et al., 2021). Berlana et al's research in 2024 also explains that parenteral administration of omega 3 fatty acids in COVID-19 patients can reduce levels of inflammatory markers such as CRP, IL-6 and CXCL10 ($p<0.05$) (Figure 1) thus providing clinical outcomes in the form of shorter ICU stay and reduced mortality (Berlana et al., 2024).

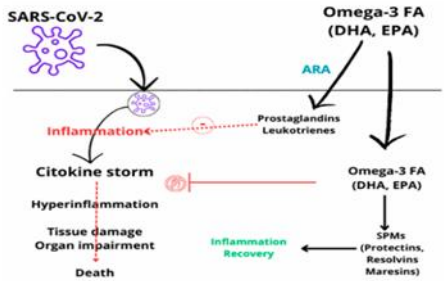

Figure 1. Mechanism of omega-3 fatty acids in lowering inflammation (Berlana et al., 2024)

A study conducted by Singer et al. (2021) found that the administration of enteral and parenteral nutrition with omega 3 fatty acids can shorten the length of treatment in the ICU room. The percentages between patients who were given omega-3 fatty acids and the control group were 31.3% and 40.4%. Meanwhile, laboratory parameters such as liver function, hematology, coagulation factors and lipid profiles showed no significant differences between the treated group and the control group. This study also did not show an improvement in cases of lung disease so omega3 did not have a better effect on patients with mild acute respiratory distress syndrome (ARDS) (Singer et al., 2021).

Research conducted by El Rhaman (2022) showed the influence of omega 3 fatty acids in the management of sepsis, which is a condition characterized by systemic inflammation and the balance of the immune system. In his study, parenteral nutrition containing omega 3 significantly reduced mortality in sepsis patients, whereas enteral nutrition did not have a significant effect on mortality. In addition, omega 3 supplementation can reduce the length of treatment in the ICU room, hospital ward so that it has benefits in the patient's recovery. Sepsis has several stages ranging from hyperinflammatory response to immunosuppression and the release of various cytokines (Wang et al., 2022). Omega 3 fatty acids have an important role in the hyperinflammatory stage. Omega 3 will help suppress the production of inflammatory

cytokines such as TNF-α, IL-1β, IL-6, and IL-10 triggered by endotoxins and exotoxins derived from pathogens. This modulation process can prevent further complications of organ dysfunction (Figure 2) (Attallah et al., 2022; Wang et al., 2022).

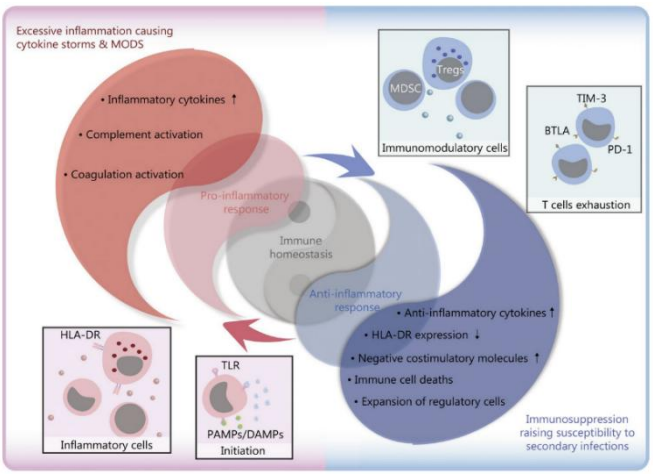

Figure 2. Diagram of the scheme of the imbalance of immune homeostasis in sepsis

The immune response begins when the host recognizes PAMP and DAMP. Inflammatory cells release pro-inflammatory cytokines and cause over-inflammation in the early stages of inflammation. Under physiological conditions, a dynamic balance between pro-inflammatory and anti-inflammatory responses maintains the homeostasis of the immune system. However, after the onset of sepsis, the balance is disturbed. Increased expression of proinflammatory cytokines released by inflammatory cells and activation of the complement and coagulation systems leads to excessive inflammation, which further leads to cytokine storms and MODS. Simultaneously or subsequently, increased release of anti-inflammatory cytokines and inhibitory molecules, decreased expression of HLA-DR, immunocyte death, and expansion of regulatory cells lead to immunosuppression, increasing susceptibility to secondary infections, which are the main causes of poor prognosis in sepsis patients (Liu et al., 2022).

Weyland et al. (2023) conducted a study on cases of indigestion. Laboratory parameters such as serum albumin, lipid profile and some inflammatory markers did not show significant results. Cuartero-Corbalán et al. (2024) also conducted a study on cases of acute abdominal disorders. The results of his study showed no significant effect on the treated group with the control group, as indicated by laboratory parameters.

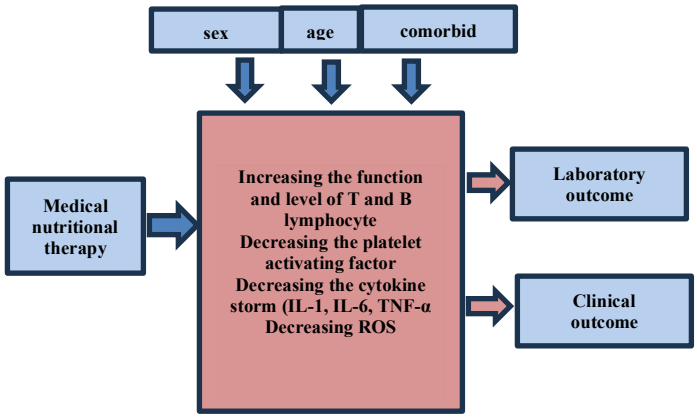

Figure 3. The concept of providing medical nutrition to the resulting clinical outcomes

The research conducted by Zhou et al. (2023) conducted studies in China and Uruguay on the administration of omega 3 nutrients in patients with burns. The results showed a decrease in the incidence of severe sepsis, septic shock and multiple organ dysfunction syndrome (MODS) in the group treated with the control group. These interventions can reduce the incidence of infection, mortality rates and reduce the length of hospital stay. Laboratory parameters showed decreased AST, ALT and GGT results, increased antioxidants and decreased inflammatory markers. This is related to a previous study conducted by Pradelli et al. (2025) that parenteral nutrition added with omega 3 to hospitalized patients can reduce the risk of infection by 40% and sepsis by 56% as well as a reduction in the duration of treatment by 2 days both in the ICU room and ward. In addition, other studies conducted by Lu et al., Wei et al. and Manzanares et al., also showed the same benefits, including a decrease in the number of complications, the number of infections and also the length of treatment so as to reduce mortality rates and are expected to reduce the incidence of malnutrition in hospitals (Figure 3) (Delfia et al., 2023).

In this literature study, there are limitations, including in some studies that sample patients in small numbers so that they cannot achieve the research objectives due to mortality that occurs before the study is completed. In addition, another factor is that the study was conducted only in one hospital where this could not be representative of the patient population, the length of the patient's previous treatment and the type of illness of the patient varied because the nutritional needs of critically ill patients depended on the severity, injury or disease and previous nutritional status. Therefore, a literature study or further research is needed to determine the effectiveness of omega 3 in curing patients with critical illnesses.

CONCLUSION

Based on this review, patients with critical illness who received enteral and parenteral nutrition enriched with omega-3 fatty acids experienced accelerated healing, reduced complication risks, and shorter ICU and ward stays compared to those who received nutrients without omega-3. However, no significant differences were observed between omega-3 and non-omega-3 nutrition in patients with indigestion or acute abdominal pain. Future research

should focus on establishing standardized omega-3 dosing and administration protocols, investigating patient-specific factors to enable personalized nutrition strategies, and conducting long-term studies on post-ICU recovery and quality of life. Additionally, exploring synergistic effects with other immunonutrients, performing cost-benefit analyses, and carefully evaluating omega-3 use in gastrointestinal disorders will help refine its role in critical care nutrition. Addressing these gaps can lead to clearer guidelines and improved outcomes for critically ill patients receiving nutritional therapy.

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